

[0028] FIGS. 19A-19D show exemplary microfluidic valves;

[0029] FIG. 20 shows an exemplary bubble vent;

[0030] FIG. 21 shows a cross-section of a microfluidic cartridge, when in contact with a heater substrate;

[0031] FIGS. 22A-22C shows various cut-away sections that can be used to improve cooling rates during PCR thermal cycling;

[0032] FIG. 23 shows a plot of temperature against time during a PCR process, as performed on a microfluidic cartridge as described herein;

[0033] FIG. 24 shows an assembly process for a cartridge as further described herein;

[0034] FIGS. 25A and 25B show exemplary deposition of wax droplets into microfluidic valves;

[0035] FIG. 26 shows an exemplary heater unit;

[0036] FIGS. 27A and 27B show a plan view of heater circuitry adjacent to a PCR reaction chamber;

[0037] FIG. 27C shows thermal images of heater circuitry in operation;

[0038] FIG. 28 shows an overlay of an array of heater elements on an exemplary multi-lane microfluidic cartridge, wherein various microfluidic networks are visible;

[0039] FIG. 29 shows a cross-sectional view of an exemplary detector;

[0040] FIG. 30 shows a perspective view of a detector in a read-head;

[0041] FIG. 31A, 31B shows a cutaway view of an exemplary detector in a read-head;

[0042] FIG. 32 shows an exterior view of an exemplary multiplexed read-head with an array of detectors therein;

[0043] FIG. 33 shows a cutaway view of an exemplary multiplexed read-head, as in FIG. 18;

[0044] FIG. 34 shows exemplary pre-amplifier circuitry for a fluorescence detector;

[0045] FIG. 35A shows effects of aperturing on fluorescence intensity; FIG. 35B shows a detector in cross section with an exemplary aperture;

[0046] FIG. 36 shows an exemplary layout for electronics and software components, as further described herein;

[0047] FIG. 37 shows an exemplary apparatus, a microfluidic cartridge, and a read head, as further described herein;

[0048] FIGS. 38-39 show positioning of a cartridge in an exemplary apparatus;

[0049] FIGS. 40 and 41 show removal of a heater unit from an exemplary apparatus;

[0050] FIGS. 42A and 42B show an exemplary heater unit and heater substrate;

[0051] FIGS. 43A and 43B show an exemplary apparatus having a detector mounted in a sliding lid;

[0052] FIGS. 44A-44C show a force member;

[0053] FIGS. 45A-45D show a force member associated with a detector;

[0054] FIG. 46 shows a block diagram of exemplary electronic circuitry in conjunction with a detector as described herein;

[0055] Additional figures are illustrated within the examples, and are further described therein.

[0056] Like reference symbols in the various drawings indicate like elements.

## DETAILED DESCRIPTION

### Overview of Apparatus

[0057] The present technology relates to a system and related methods for amplifying, and carrying out diagnostic analyses on, polynucleotides (e.g., a DNA, RNA, mRNA, or rRNA) from biological samples. For example, the system and methods can determine whether a polynucleotide indicative of the presence of a particular pathogen (such as a bacterium or a virus) can be present. The polynucleotide may be a sample of genomic DNA, or may be a sample of mitochondrial DNA. The nucleotides are typically provided to the system having been isolated or released from particles such as cells in the sample. The system includes a disposable microfluidic cartridge containing multiple sample lanes in parallel and a reusable instrument platform (a PCR analyzer apparatus) that can actuate on-cartridge operations, can detect (e.g., by fluorescence detection) and analyze the products of the PCR amplification in each of the lanes separately, in all simultaneously, or in groups simultaneously, and, optionally, can display the results on a graphical user interface.

[0058] A system, microfluidic cartridge, heater unit, detector, kit, methods, and associated computer program product, are now further described.

[0059] By cartridge is meant a unit that may be disposable, or reusable in whole or in part, and that is configured to be used in conjunction with some other apparatus that has been suitably and complementarily configured to receive and operate on (such as deliver energy to) the cartridge.

[0060] By microfluidic, as used herein, is meant that volumes of sample, and/or reagent, and/or amplified polynucleotide are from about 0.1  $\mu$ l to about 999  $\mu$ l, such as from 1-100  $\mu$ l, or from 2-25  $\mu$ l. Similarly, as applied to a cartridge, the term microfluidic means that various components and channels of the cartridge, as further described herein, are configured to accept, and/or retain, and/or facilitate passage of microfluidic volumes of sample, reagent, or amplified polynucleotide.

[0061] FIG. 1 shows a perspective view of an exemplary apparatus 100 consistent with those described herein, as well as various components thereof, such as exemplary cartridge 200 that contains multiple sample lanes, and exemplary read head 300 that contains detection apparatus for reading signals from cartridge 200. The apparatus 100 of FIG. 1 is able to carry out real-time PCR on a number of samples in cartridge 200 simultaneously. Preferably the number of samples is 12 samples, as illustrated with exemplary cartridge 200, though other numbers of samples such as 4, 8, 10, 16, 20, 24, 25, 30, 32, 36, 40, and 48 are within the scope of the present description. In preferred operation of the apparatus, a PCR-ready solution containing the sample, and, optionally, one or more analyte-specific reagents (ASR's) is prepared, as further described elsewhere (see, e.g., U.S. patent application publication 2006-0166233, incorporated herein by reference), prior to introduction into cartridge 200. An exemplary kit for preparing a PCR-ready sample, for use with the system described herein, the kit comprising buffers, lysis pellets, and affinity pellets, is shown in FIG. 2.

### System Overview

[0062] A schematic overview of a system 981 for carrying out analyses described herein is shown in FIG. 3. The geometric arrangement of the components of system 981 shown